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A Review On The Toxicological Implication Of Cosmetic, Hair Dyes And Relaxers.

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Abstract.

The use of cosmetic products is on the increase worldwide and the variety of chemical compounds used in the manufacture of these products is also on the increase. As a result, the risks of intoxication, allergy, and indiscriminate use are also increased. This work aims to highlight the biological risks that cosmetics pose to human health because of the toxic substances used in most formulations. This study attempts to relate the main toxic chemical substances present in cosmetic products to the possible health implications. Despite the toxicities associated with cosmetic usage, the cosmetics, and "makeup" industries enjoy wide acceptability irrespective of age and sex. Studies on the possible toxicities of cosmetics have caused the ban in many countries on poisonous substances in cosmetic products. Among substances suspected of toxicity in cosmetic products are lead, chromium, nickel, mercury, arsenic, cadmium, hydroquinone, steroids, and nitrosamine. Surprisingly, most of these substances with toxic potentials are still used in the manufacturing of many cosmetics in use today. When the levels of these substances exceed regulatory values, pathologies such as cancers, renal disorders, thinning and easy brushing of the skin, dermatophyte infection with lesions, macular hyperpigmentation, pityriasis vesicular, diabetes mellitus, maculopapular eruption, hypertension are the possible result. Toxicological and health hazards associated with cosmetic use can be minimized by adherence to regulatory policies, use of non-toxic alternatives in formulations, the addition of active anti-toxic substances, limiting the quantity used, and constant monitoring of adverse effects after use.

1. INTRODUCTION

"Toxicology is the study of the adverse physicochemical effects of chemical, physical or biological agents on living organisms and the ecosystem, including the prevention and amelioration of such adverse effects."-American Society of Toxicologists. Examples of such agents include cyanide (chemical), radiation (physical), and snake venom (biological). Toxicology can be defined as that branch of science that deals with poisons and a poison can be defined as any substance that causes a harmful effect when administered, either by accident or by design, to a living organism. By convention, toxicology also includes the study of harmful effects caused by physical phenomena, such as radiation of various kinds, noise, and so on. In practice, however, many complications exist beyond these simple definitions, both in bringing a more precise definition to the meaning of poison and the measurement of toxic effects. Broader definitions of toxicology, such as "the study of the detection, occurrence, properties, effects, and regulation of toxic substances," although more descriptive, do not resolve the difficulties. Toxicity itself can rarely, if ever, be defined as a single molecular event, but is, rather, a cascade of events starting with exposure, proceeding through distribution and metabolism, and ending with interaction with cellular macromolecules (usually DNA or protein) and the expression of a toxic endpoint (Figure 5). This sequence may be mitigated by excretion and repair (Hodgson, 2010).

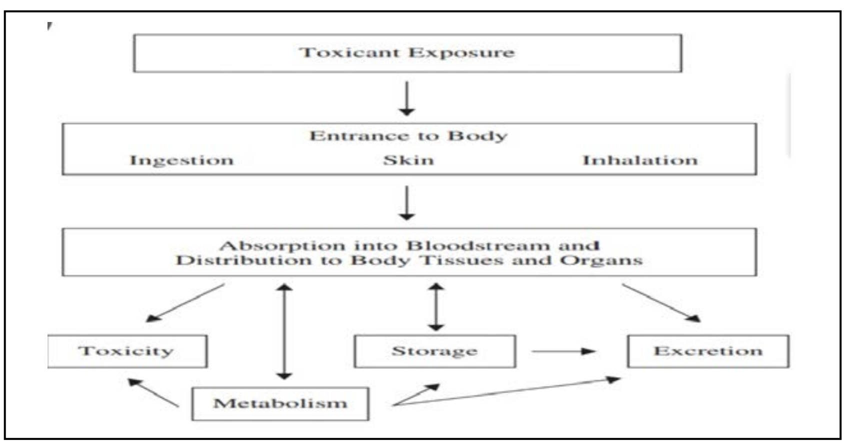

Figure 1; Fate and effect of toxicants in the body (Hudgson, 2010).

New research shows that health-related complaints about cosmetic products like shampoo and makeup are at an all-time high since the U.S. Food and Drug Administration (FDA) began keeping track more than a decade ago. That's concerning because when cosmetic products cause health issues, addressing the problem or even getting a potentially unsafe product off the market isn't a simple process. Cosmetics also do not need to go through a pre-market approval process before they are sold in stores, and regulators do not assess the safety and effectiveness of the claims on the products. Instead, people and doctors are asked to report any health complications to the FDA's database (called the Centre for Food Safety and Applied Nutrition's Adverse Event Reporting System, or CFSAN). If the FDA sees any increases that warrant concern, they can investigate (Sifferlin, 2019). However, most toxic cosmetic products are very much still in circulation in the market and used daily by both males and females which can cause adverse toxicological implications like alopecia, baldness, and in severe cases hormone imbalance and infertility (Sifferlin, 2019).

Cosmetics is a Greek word that means to 'adorn' (addition of something decorative to a person or a thing). It may be defined as a substance that comes in contact with various parts of the human body like skin, hair, nail, lips, teeth, mucous membranes, etc, The Pharmaceutical Affairs Act defines cosmetics as "Articles with mild action on the human body, which are intended to be applied to the human body through rubbing, sprinkling or other methods, aiming to clean, beautify and increase the attractiveness, alter the appearance or to keep the skin or hair in good condition". The most popular cosmetics are hair dyes, powders, and creams (Gaurav et al., 2018). Examples of Cosmetics: Skin-care creams, powders, lotions, lipsticks, nail polishes, eye and face makeup, deodorants, baby products, hair colorants, sprays, etc.

1.1. The link between cosmetics and toxicity.

The study of more than 1,100 hair products marketed toward black consumers revealed a shocking bias in the products' chemical composition. Less than one in four products tested "low hazard" for the inclusion of dangerous ingredients, with most containing toxic chemicals that can potentially cause cancer or developmental and reproductive damage, disrupt hormones, and trigger other adverse health effects. Toxic ingredients such as lye (found in relaxers) and formaldehyde (found in keratin straightening treatments and Brazilian blowouts) are still commonly used in black hair salons. Terms like natural and organic are highly subjective scientifically, and clever wording allows companies to slip in all kinds of dangerous chemicals. "There are a lot of chemicals in the periodic table that is technically 'natural'" (Cagle, 2018).

Brooks points out. "Ammonia is natural, Alcohol is natural, and Companies will put a little bit of aloe or olive oil into a product and call it organic but all the bad stuff is still there too." Case in point: Relaxers, by far the most hazardous product tested, is now branded by cosmetic companies as safe if they contain no lye, yet the EWG analysis found that many companies merely replaced the lye with calcium hydroxide, a caustic irritant (Cagle, 2018).

Cosmetics and personal care products are ubiquitous. The US researchers identified some 12500 industrial chemicals used as cosmetic ingredients, including carcinogens, pesticides, reproductive toxins, endocrine disruptors, plasticizers, degreasers, and surfactants. The US FDA estimated 12,500 chemicals used in cosmetics, 20% of them are safe according to a CIR review, only 11 of them are banned in the US but more than 1300 are banned or restricted in the EU. Heavy metals such as lead, mercury, cadmium, arsenic, and nickel, as well as aluminum, classified as light metal, are detected in various types of cosmetics (color cosmetics, face, and body care products, hair cosmetics, herbal cosmetics, etc.). The metals are from the contamination of raw materials and use of sub-standard raw materials, lack of compliance by small-scale manufacturers, and lack of strict regulations. Also, Alam et. al, 2019 many cosmetic products contain heavy metals as ingredients or impurities. Vella et. al, 2019 reported the presence of lead in toothpaste is beyond the limit of US and EU standards. According to Panico et. al, 2019 PEGs (favorably used as penetration enhancers)may contain residual impurities like lead, iron, cobalt, nickel, cadmium, and arsenic (Mohiuddin, 2019).

2. CHEMICALS USED IN THE PRODUCTION OF HAIR DYES, HAIR RELAXERS, AND COSMETICS, AND THEIR TOXICITY.

2.1. BUTYLATED COMPOUNDS

Butylated hydroxyanisole (BHA) and butylated hydroxytoluene (BHT) are used as preservatives in a variety of personal care products (lip and hair products, makeup, sunscreen, antiperspirants, deodorants, fragrances, creams), BHT is a toluene-base ingredient. The European Commission on Endocrine Disruption has determined that there is strong evidence that BHA is a human endocrine disruptor. A study carried out in normal mammalian kidney cells found that exposure to BHA caused specific damage at the cellular level and was found to exert a significant cytotoxic effect even at low doses. The International Agency for Research on Cancer (IARC) determined that there was only limited evidence of carcinogenicity for products used on the lips. There is moderate evidence that BHT is a human respiratory irritant (Petric, 2019).

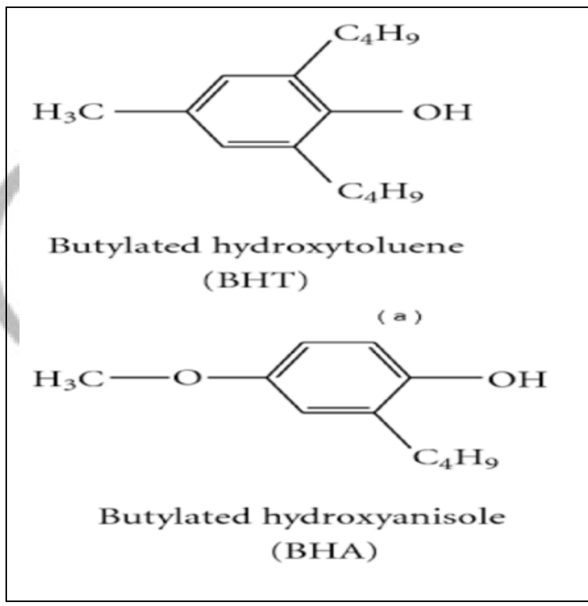

Figure 2: Chemical structure of Butylated Compounds. (source: www.ewg.org)

The toxicological implication of BHA

i. Endocrine disruption: The European Commission on Endocrine Disruption has determined that there is strong evidence that BHA is a human endocrine disruptor.

ii. Toxicity: Environment Canada Domestic Substance List has classified BHA as a high human health priority (www.ewg.org). A study carried out in normal mammalian kidney cells found that exposure to BHA caused specific damage at the cellular level and was found to exert a significant cytotoxic effect even at low doses (Labrador et al, 2007). The Environment Canada Domestic Substance List has classified BHT as expected to be toxic or harmful (www.ewg.org). A safety assessment of BHT reported that BHT applied to the skin of rats was associated with toxic effects on lung tissue, but judged that the low concentrations used in cosmetics were safe (Campaign for safe cosmetics, 30-Jan-2020).

iii. Developmental and reproductive toxicity: Studies carried out in rats found that exposure to high doses of BHA resulted in weak dysfunction and underdevelopment of the reproductive systems of both male and female rats. Changes in testosterone levels, sex weight organs, and sexual maturation were also observed (Campaign for safe cosmetics, 30-Jan-2020)

iv. Cancer: The National Toxicology Program (NTP) Report on Carcinogens, 12th Edition, reports that BHA is reasonably anticipated to be a human carcinogen based on sufficient evidence of carcinogenicity from animal studies. The California EPA's Proposition 65 list also identifies BHA as a possible human carcinogen and requires labeling for products that are used on the lips, while the International Agency for Research on Cancer (IARC) determined that there was only limited evidence of carcinogenicity for products used on the lips (www.ewg.org). One study found that dietary exposure to BHA caused both benign and malignant tumors in the stomachs of rats, mice, and hamsters. However, another study determined that typical dietary levels of BHA did not increase the incidence of stomach cancer (campaign for safe cosmetics, 30-Jan-2020).

v. Irritation: The American Conference of Governmental Industrial Hygienists (ACGIH) has determined that there is moderate evidence that BHT is a human respiratory irritant (campaign for safe cosmetics, 30-Jan-2020).

2.2. COAL TAR

Coal tar is a known human carcinogen found in shampoos and scalp treatments, soaps, hair dyes, and lotions. Coal Tar is a thick liquid or semi-solid extracted from bituminous coal, it is a complex mixture of hundreds of compounds, many of which are polycyclic aromatic hydrocarbons. Occupational exposure to coal tar which is used in the production of shampoos and scalp treatments, soaps, hair dyes, and lotions, increases the risk of skin cancer. Other types of cancer (lung, bladder, kidney, and digestive tract cancer) have also been linked to occupational exposure to coal tar and coal-tar pitch. Pyridine, a coal tar constituent, has been linked to neurological damage. Effects include emotional and sleep disturbances, as well as loss of coordination (Petric, 2019). The quality of coal tar dye also helps to act as a binding agent for liquids. It's used to help strengthen the 'hold' that a color has once it's been applied to your body (Backe, 2018).

Physical and Chemical Properties

Coal Tar is a nearly black, viscous liquid, heavier than water, with a naphthalene-like odor and a sharp burning taste (Gennaro1990). The composition of Coal Tar is variable, but generally, it consists of 2% to 8% light oils (benzene, toluene, xylene);8% to 10% middle oils (phenols, cresols, and naphthalene);8% to 10% heavy oils (naphthalene and derivatives); 16% to20% anthracene oils (mostly anthracene); and about 50% pitch(Gosselin et al. 1984). Coal Tar is "practically insoluble" in water; however "all or almost all" dissolves in benzene or nitrobenzene (Budavari, 1989).

The toxicological implication of coal tar

i. Cancer: Experimental studies have found that exposure to and application of coal tar produce skin tumors. Coal tar has also been associated with cancer of the lung, bladder, kidney, and digestive tract. Benzopyrene, a constituent of coal tar, is carcinogenic through skin exposure.

There have been many reports of skin cancer among patients using therapeutic coal-tar preparations (http://www.safecosmetics.org)

ii. Organ System Toxicity: Pyridine, a coal tar constituent, has been linked to neurological damage. Effects include emotional and sleep disturbances, as well as loss of coordination.

iii. Brain damaging: Ingesting them over a continuous amount of time can potentially cause brain damage or speed up the progression of brain diseases like Alzheimer's (Backe, 2018). These colors may be contaminated with low levels of heavy metals and some are combined with aluminum substrate. Aluminum compounds and many heavy metals are known to be harmful to the brain, Aluminum inhibited both the cytosolic and mitochondrial hexokinase activities in the brain, and inhibition of carbohydrate utilization may be one of the mechanisms by which Aluminum can act as a neurotoxin.

2.3. ETHANOLAMINE COMPOUNDS

Ethanolamine compounds are present in soaps, shampoos, hair conditioners and dyes, lotions, shaving creams, paraffin and waxes, household cleaning products, pharmaceutical ointments, eyeliners, mascara, eye shadows, blush, make-up bases, foundations, fragrances, and sunscreens. The European Commission prohibits diethanolamine (DEA) in cosmetics, to reduce contamination from carcinogenic nitrosamines that are formed after the reaction of DEA with other ingredients DEA and TEA (triethanolamine) has been found to be hepatocarcinogenic in female mice (Petric, 2009).

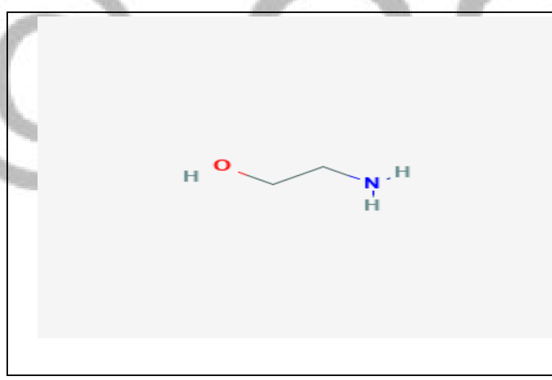

Figure 3: Chemical structure of Ethanolamine (source:).

The toxicological implication of Ethanolamine compounds

i. Studies have found that DEA affects human male reproductive health. It alters sperm structure, causing abnormalities that affect the sperm's ability to swim and fertilize the egg (Panchal et al., 2013).

ii. DEA accumulates in the liver and kidney, causing organ toxicity.

iii. It also has possible neurotoxic effects such as tremor

iv. Another study suggests that memory function and brain development in offspring could be permanently affected by mothers' exposure to DEA (Craciunescu et al., 2006).

2.4. ETHOXYLATED

Ethoxylated ingredients are found in shampoo, bath soap, bubble baths, and hair relaxers. Ethoxylated ingredients are generally of low concern on their own, but they can be contaminated with ethylene oxide, a known human carcinogen. Lymphoma and leukemia are the cancers most frequently reported to be associated with occupational exposure to ethylene oxide, but the stomach and breast cancers may also be associated with it.

2.5. FORMALDEHYDE AND FORMALDEHYDE DONORS

Formaldehyde is a preservative that can irritate skin, eyes, nose, and, the respiratory tract, and can cause cancer among those with high levels of exposure. Small amounts are permitted for use in cosmetics, and it's mainly found in hair straighteners (relaxers) and nail polish/hardeners. Some chemicals react to release ('donate') formaldehyde, including DMDM hydantoin, quaternium-15, Diazolidinyl urea, and imidazolidinyl urea. People allergic to formaldehyde are often allergic to these formaldehyde donors and are advised to avoid these chemicals, particularly in leave-on products (Bray, 2016).

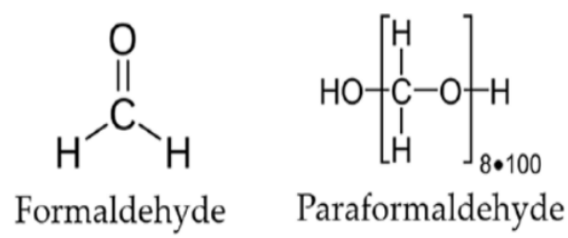

Figure 4: Chemical structure of Formaldehyde (source http://www.ewg.org).

2.6. P-PHENYLENEDIAMINE

PPD is an aromatic amine compound; its chemical formula is $C_6H_8N_2$ and its molecular weight is 108.15 g/mol. It is a white to light purple powder that darkens on exposure to air (it oxidizes, turning first red, then brown then finally black); it is slightly soluble in water, It is primarily used as an ingredient of oxidative hair coloring products. P-phenylenediamine is one of many coal-tar colors, which are derived from petroleum. PPD reacts with hydrogen peroxide to bind the color to the hair permanently. It is also often mixed with other chemicals, such as resorcinol, to achieve a particular color of dye.

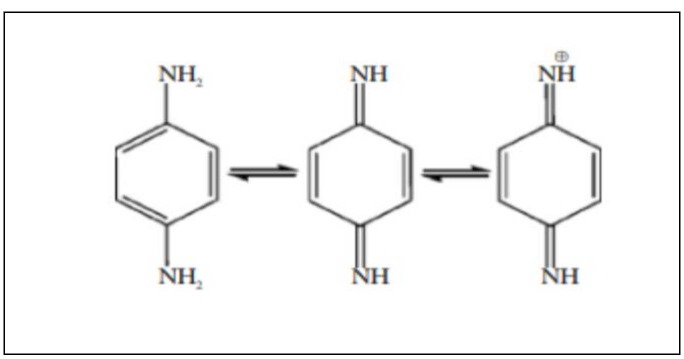

Figure 5: Reaction mechanism of P-Phenyladiamine (source:Mechanism of hair dying and their safety aspects).

The toxicological implication of P-phenylenediamine

a. Birth defects

b. Skin irritation

c. Liver and blood toxicity

d. A mild reaction to hair dye in a client usually presents as an itchy dry rash on the upper eyelids (see eyelid dermatitis) and/or the rims of the ears.

e. More severe reactions cause marked reddening, blistering, and swelling of the eyelids, scalp, face, and neck.

f. High concentrations of PPD in black temporary tattoos may result in intense blistering reactions at the site of the tattoo within 1–2 days of tattooing; a lichenoid eruption may arise 1–2 weeks later.

g. Dermatitis may become widespread, due to direct contact or to autoeczematisation.

h. People working with PPD, such as hairdressers may develop hand dermatitis. Dermatitis may spread to the arms, chest, and elsewhere due to autoeczematisation.

i. Dermatitis may be followed by post-inflammatory hyperpigmentation, hypopigmentation, or scarring.

j. After the reaction subsides, lifelong sensitization to PPD is likely.

k. Pharyngeal, laryngeal irritation; bronchial asthma; sensitization dermatitis

Figure 6: Contact allergy to P-Phenyladiamine in hair dye (source:www.dermetnz.org).

2.7. PARABENS

Parabens are homologous esters of para-hydroxybenzoic acid. Parabens; are cheap preservatives used in a wide range of cosmetic products. They prevent bacteria, mold, fungus, and even parasites from growing. Almost 60% of all cosmetic products contain parabens (Elizabeth, 2019).

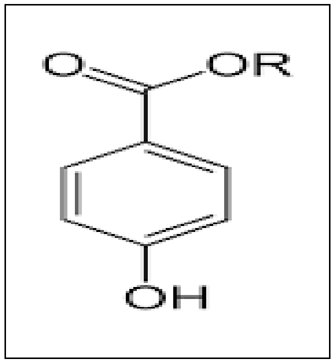

Figure 7: Chemical structure of paraben (source;https://en.m.wikipedia.org/wiki/Paraben).

2.8. PETROLEUM & MINERAL OILS (PETROCHEMICALS)

Used in skin care products for a variety of reasons, petrochemicals have been linked to major health concerns. Petroleum-based products can be contaminated with dozens of toxic chemicals, some known to cause cancer and damage nerves. 22% of beauty products contain toxic levels of these harmful chemicals. Petroleum-based ingredients can also penetrate the skin, causing further health hazards. A 2009 study showed that using mineral oil products has the potential to increase the rate of tumor growth (Elizabeth, 2019).

2.9. HYDROQUINONE

Hydroquinone, known as benzene-1,4-diol or quinol, is an aromatic organic compound that is a type of phenol. Its chemical structure features two hydroxyl groups bonded to a benzene ring in a para position. In a substituted form, the derivatives of the compound can still be referred to as hydroquinone. Since it is weakly acidic, the reactivity of OH groups of these compounds compares well with other phenols. Its conjugate base can easily undergo O-alkylation to produce mono- and diethers. In the same way, hydroquinone is highly susceptible to ring substitution by Friedel-Crafts reactions such as alkylation. This reaction is used to produce much-known antioxidants such as 2-tert-butyl-4-methoxyphenyl ('BHA'). A very important dye quinizarin is produced by the diacylation reaction of hydroquinone with phthalic anhydride [30], but the most important reaction is the conversion of hydroquinone to produce mono- and diamino derivatives methylaminophenol, used in photography.

$$C_6H_4(OH)_2 + CH_2\ NH_2 \text{----->} C_6H_4(OH)(N(H)CH_3) + H_2O \quad (1)$$

Also, diamines which are useful in the rubber industry as anti-ozone agents can be produced from aniline:

$$C_6H_4(OH)_2 + 2C_6H_5NH_2 \text{------->} (N(H)\ C_6H_5)_2 + 2H_2O \quad (2)$$

The compound is variously used, mainly with its action as a reducing agent that dissolves in water. It is widely used in most photographic development for film and paper. It can act as an inhibitor by preventing the polymerization of acrylic acid, methyl methacrylate, cyanoacrylate, and other monomers that can respond to free radical initiated joining. This reaction utilizes the antioxidant properties of hydroquinone to undergo mild oxidation and convert to the compound parabenzoquinone, $C_6H_4O_2$, often called p-quinone or quinone. This reaction is reversible as reduction (www cosmeticsafety.org).

2.10. SODIUM HYDROXIDE

Sodium Hydroxide, Calcium Hydroxide, Magnesium Hydroxide, and Potassium Hydroxide are white solids that occur in several forms, including powders. In cosmetics and personal care products, Sodium, Calcium, Magnesium, and Potassium Hydroxide are used in the formulation of bath products, cleansing products, hair dyes, etc. Sodium and Calcium Hydroxide is also used in hair straighteners (relaxers) and hair wave sets. Sodium Hydroxide, Calcium Hydroxide, Magnesium Hydroxide, and Potassium Hydroxide are used to control the pH of cosmetics and personal care products. Magnesium Hydroxide is also used as an absorbent (www cosmeticsafety.org).

The use of sodium hydroxide-based hair straighteners/relaxers can have the following effects:

i. Sodium hydroxide is very corrosive and can cause severe burns in all tissues that come in contact with it. Inhalation of low levels of sodium hydroxide as dust, mists, or aerosols may irritate the nose, throat, and respiratory airways. Inhalation of higher levels can produce swelling or spasms of the upper airway leading to obstruction and loss of measurable pulse; inflammation of the lungs and accumulation of fluid in the lungs may also occur." (ATSDR report, 2009).

ii. It can easily dissolve through surfaces like fabric, plastic, and even the skin. When it seeps through the hair, it breaks the natural bonds that are meant to protect the hair, altering its natural structure.

iii. Continual use of a relaxer can cause alopecia where hair follicles are damaged beyond repair or completely wiped out. This can lead to one being completely bald.

iv. Scalp irritation, skin burns, permanent scarring, deep ulcerations, skin drying and cracking, dermatitis, irreversible baldness, eye damage including blindness, and weak, dry, broken, and damaged hair (ARSO, 2015).

2.11. LEAD ACETATE

Lead Acetate is used as a color additive for the dark shade hair dyes. It is said to cause anemia and produce neurological problems.

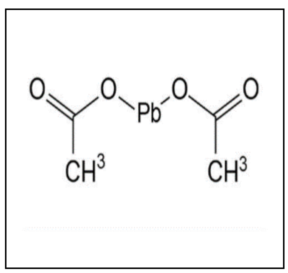

Figure 8: Chemical formulas of lead acetate (source; www.chemspider.com)

Toxicological Implication of Lead Acetate.

i. They are readily absorbed through the skin capable of traveling to various organs in the body, including the brain, and are reasonably believed to be carcinogenic

ii. Lead acetate is a known neurotoxin

iii. According to the Centers for Disease Control and Prevention Trusted Source (CDC), lead poisoning can lead to brain and nervous system damage, slowed growth, and learning disabilities.

2.12. RESORCINOL

Resorcinol can be regarded as a phenol derivative in which a hydrogen atom is substituted by a hydroxyl group in the meta position to the OH. Its chemical structure is shown in Figure 13. Resorcinol is a toxic dye that can cause scalp irritation and is an allergen affecting the endocrine system. Resorcinol is commonly used in hair dyes and acne medication. In higher doses, it is toxic and can disrupt the function of the central nervous system and lead to respiratory problems. It has also been shown to disrupt the endocrine system, specifically thyroid function. Irritation of eyes, skin, nose, throat, upper respiratory system; bluish skin, dizziness, drowsiness. (www.ewg.org).

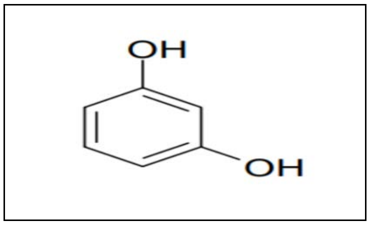

Figure 9: Chemical structure or resorcinol (source;http.ewg.org).

2.13. MERCURY (HG)

Mercury has no positive role in the human body; in fact, a safe level of mercury exposure is very difficult to determine. It can be present in the environment in several different forms, and while all forms of mercury are toxic to humans, the pattern of toxicity varies with its chemical form, the route of exposure, the amount, duration, and timing of exposure, and the vulnerability of the person exposed (Hamsi et al., 2012).

The toxicological implication of Mercury

a. Nervous system – developmental delays, impaired vision and hearing, motor function, brain function, IQ

b. Cardiovascular system – High blood pressure, altered heart rate, increase heart attack risk.

c. Effects on the immune and reproductive systems, liver, and kidneys.

d. It causes skin dryness and spots, and pimples.

e. It affects the brain of an unborn child.

f. It affects the reproductive organs which leads to infertility.

AHT (2004) reports that of the more than 10,000 ingredients used in personal care products, some are linked to cancer, birth defects, developmental and reproductive harm, and other health problems that are on the rise. Table 1 shows a sample of ingredients contained in some cosmetics and their associated health impacts.

Table 2: Hazardous chemicals in cosmetics (AHT, 2004)

Chemicals	Hair Products	Toxicity effect.
Coal tar colors	Make-up and hair-dye	Some FD&C colors are carcinogenic or contain impurities that have been shown to cause cancer when applied to the skin.

		Allergens and irritants.
Diethanolamine(DEA)	Widely used in shampoo	A suspected carcinogen, its compounds, and derivatives include triethanolamine (TEA), which can be contaminated with nitrosamines shown to cause cancer in laboratory animals. [Suggestive animal evidence]
Formaldehyde and its releasers	Eye shadow, mascara, nail polish, shampoo, blush, etc.	Carcinogen, a reproductive toxin, is shown to cause or exacerbate asthma and other respiratory ailments. [Strong animal and human evidence]
Glycol Ethers	Nail polish, deodorant, perfume	Hazardous to the reproductive system. Other effects include anemia and irritation of the skin, eyes, nose, and throat. EGPE, EGME, EGEE, DEGBE, PGME, DPGME, and others with "methyl" in their names. [Strong animal and human evidence]
Lead	Hair dyes (e.g. Grecian formula) and in eye makeup (as a preservative)	Lead damages the nervous system, leading to decreased learning ability and behavioral deficits. Reproductive toxin. Carcinogen. [Strong animal, human, and children evidence]
Mercury	Skin-lightening cream and in eye makeup (as a preservative).	Mercury is toxic to development, as well as to the nervous system, and is suspected to have harmful effects on the respiratory system, the kidneys, and gastrointestinal and reproductive systems. [Strong animal, human, and children evidence]
Parabens	Hair products (shampoo, conditioners, styling products), soaps, body washes, moisturizers, shaving cream, gels, cosmetics/makeup.	Methyl-, ethyl-, propyl-, butyl-, isobutyl- and other parabens, have shown hormonal activity. The most common preservatives used in cosmetics. Recently found in tissue samples from human breast tumors. Propylparaben affects sperm production in juvenile rats. [Suggestive animal and human evidence]
Phenylenediamine(PPD)	Hair dyes (oxidation dyes, amino dyes paradyes, or peroxide dyes)	PPD is mutagenic and reasonably anticipated to be a human carcinogen. It has been banned in Europe. It is also linked with skin irritations and respiratory disorders. [Compelling animal evidence]
Phthalates Most used in	Fragrance, perfume,	Liver and kidney lesions: reproductive

cosmetics:DBP, DMP, and DEP.	deodorant, nail polishes, various hair products, cream, lotion, etc.	abnormalities, including testicular atrophy, altered development of reproductive tissues and subtle effects on sperm production (maybe through endocrine disruption); cell line transformations; and cancers, including those of the liver, kidney, and mononuclear cell leukemia. These effects are generally quantitatively though not qualitatively different between phthalates. The developing male reproductive system appears to be sensitive. [Strong animal evidence; suggestive human evidence; some children evidence through exposure via medical devices]

Other toxic chemicals used in cosmetic production are;

a. Retinal Palmate.

b. Phenacetin.

c. Chromium.

d. Cadmium and its compound.

e. Arsenic.

f. Methylisothiazolinone.

3. HOW COSMETICS CAUSE TOXICITY

Absorption of lead into the skin is governed by chemical structure; therefore, skin organic lead absorption into the body tissues is more rapid than with inorganic lead compounds because of greater lipid solubility; large amounts of lead gain access to nerve tissue. Acute effects of lead intake are ataxia, headache, vomiting, stupor, hallucination, tremors, and convulsions. Chronic cases include weight loss, anemia, kidney damage, and memory loss. Lead bioaccumulates in bones and teeth, and it is classified as an environmental priority pollutant by the US EPA (Nduka et al., 2019)

Skin contact with nickel can cause dermatitis, and a type of chronic eczema known as 'nickel itch' is caused by hypersensitivity reactions to nickel on the skin. Oral toxicity of nickel is very low, but ingestion results in hyperglycerine and depression of the central nervous system. Large dose inhalation of nickel dust can cause lung and sinus cancer in humans. Nickel and certain of its compounds are listed by International Agency for Research on Cancer (IARC) under group 2B carcinogens as possibly carcinogenic to humans (Nduka et al., 2019)

Cr^{6+} is regarded as a cancer-causing agent and is toxic. It is corrosive to skin and causes denaturation and precipitation of tissue proteins. Chronic exposure may lead to cancer of the respiratory tract and should be controlled in such a manner that no person is exposed to carcinogenic chromium (VI) at concentrations greater than 25 mg/m3 of air, determined as the time-weighted average (TWA) concentration limit for up to a 10-hour workday or a 40-hr work week, over a working lifetime. Chronic inhalation of manganese dust or fumes can cause manganism, a nonfatal disease that affects the central nervous system. The symptoms are mental disorders and disturbance in speech (Nduka et al., 2019).

Mercury can cause both chronic and acute poisoning. Case-control studies have shown effects such as tremors, impaired cognitive skills, and sleep disturbance in workers with chronic exposure to mercury vapor even at low concentrations in the range of 0.7–42 μg/mg. A study has shown that acute exposure (4–8 hours) to calculated elemental mercury levels of 1.1–44 mg/m3 resulted in chest pain, dyspnoea, cough, hemoptysis, impairment of pulmonary function, and evidence of interstitial pneumonitis. Occupational exposure has resulted in broad-ranging functional disturbance, including erythrism, irritability, excitability, excessive shyness, and insomnia. In regular and consistent use, a fine tremor develops and may escalate to violent muscular spasms. Long-term, low-level exposure has been associated with more subtle symptoms of erythrism, including fatigue, irritability, loss of memory, vivid dreams, and depression (Nduka., 2019).

In 2006, the United States Food and Drug Administration revoked the approval of the use of hydroquinone and proposed a ban on all over-the-counter preparations, because it felt that hydroquinone cannot be ruled out as a potential carcinogen. The reason was based on the absorption in humans and the incidence of neoplasm in rats shown by several studies in which adult rats showed increased rates of tumor development (Nduka, 2019). Extensive literature documentation reveals that hydroquinone can cause exogenous ochronosis, a disease that deposits blue-black coloration on the skin if taken orally; but skin preparations containing the ingredient are administered topically. Although proper use of hydroquinone as a skin lightening agent can be effective, it causes skin sensitivity. The effect can be minimized by the daily use of sunscreen with a high persistent pigment darkening (PPD) rating. Hydroquinone can be combined with alpha hydroxy acids which exfoliate the skin to quicken the lightening process. In the United States, skin creams usually contain up to 2% of hydroquinone, but higher amounts of up to 4% or above should be prescribed and used with caution (Nduka, 2019).

The most trending research and publication that minor constituents of other chemicals such as phthalates, parabens, and, phenols in personal care products (shampoos, toothpaste, soap, etc.), though not extensively discussed, can cause early puberty in young girls and boys. The chemicals can enter the body by cutaneous penetration through the skin, inhalation, or, accidental ingestion. A worrisome aspect is that exposure is very much possible through mothers during pregnancy and breastfeeding (Nduka, 2019).

Chemical hair straightening is a process of changing naturally curly or kinky hair to permanent straight hair using chemical agents. Chemical relaxers used on the hair in contain sodium, potassium, or guanine hydroxides, sulfites, or thioglycolates. All these chemicals work to produce a straight appearance by affecting the cysteine disulfide bonds of the hair. This process weakens the hair shaft, as the rearrangement of disulfide bonds does not occur without structural damage to the shaft and a decrease in tensile strength compared to untreated hair (Olasode, 2009). The process leaves the hair dry, weak and susceptible to breakage. Hair breakage, hair thinning, lack of hair growth, scalp irritation, scalp damage, and hair loss are some of the complaints from many who experience problems due to the misuse or chronic use of chemical hair relaxers. Allergic contact dermatitis to thioglycolate products has been reported complications of chemical hair straight with potent chemicals include dilapidation, traumatic hair breakages, hair discoloration from bleaching, scalp abrasions, and sores and burns, especially with chemicals with unacceptably high pH. One of the concerns is the change in hair's pH level. Hair in a healthy state should have a pH of 4.5-5.5. Hair's natural oil, sebum, has a pH of 5. On the pH scale of between 1 being the most acid and being the most alkaline, relaxers have a pH of between 8.4 and 14, thus changing hair's naturally slightly acid state to alkaline. This will cause the hair to feel dry, and coarse, and in extreme cases cause hair breakage. Necrosis of the scalp has been reported. Chemical hair relaxers have been documented to cause alopecia (Olasode, 2009).

3.1. TOXICITY CAUSED BY COSMETIC USE

Due to the presence of numerous components in the formulation of cosmetic products, such products have the potential to cause side effects and their consequences can range from a simple mild hypersensitivity reaction to an anaphylactic process or even a lethal intoxication (Draelos, 2015).

There are many types of adverse reactions caused by cosmetics. Most adverse reactions are irritant, however, type IV hypersensitivity, contact urticaria, photosensitization, pigmentary disorders, damage to hair and nails, paronychia, acneiform eruptions, folliculitis, and exacerbation of an established dermatosis may also occur. Side effects of cosmetic products do occur. It is to be expected that the improvements in safety, tolerance, and skin compatibility will not prevent the side effects of cosmetic products from increasing in the future because of the continuing goals to intensify their biological activity and therapeutic efficacy (Pereira et al., 2018).

The main chemical elements present in the hair are composed of carbon (45%), oxygen (28%), nitrogen (15%), hydrogen (6.7%), and sulfur (5.3%). Moreover, various trace elements are present (these can be found by performing a trace mineral analysis): Ca, Mg, Sr, B, Al, Si, Na, K, Zn, Cu, Mn, Fe, Ag, Au, Hg, As, Pb, Sd, Ti, W, Mo, I, P, Se. It is important to remember that the percentages of trace elements present in the hair are subjective and vary in each individual. Cystine is the main amino acid present in keratin (17.5%), followed by serine (11.7%) and glutamic acid (11.1%). Threonine, arginine, and glycine are instead present in smaller percentages (approximately 6%). 80% of the weight of the hair is due to the presence of protein (amino acid polymers), among which the main one is keratin, composed of 18 amino acids. The main amino acids that make up keratin are cysteine (17.5%), serine (11.7%) glutamic acid (11.1%), threonine (6.9%), and glycine (6.5%), and lastly arginine (5.6%) (Marco et al., 2018).

Many scientists reviewed the general toxicology of hair dyes and mutagenicity-carcinogenicity of hair dyes and they have reported clinical observations of adverse reactions to hair dyes. The primary toxicological concerns of hair dyes, primarily oxidation hair dyes, are contact dermatitis and long-term "potential" systemic effects. The para diamine oxidation derivative dyes are having more sensitizing potential when compared to other amine derivatives. P-Phenylenediamine is the major component of oxidation hair dyes and oxidation dyes are the most widely used of all hair dyes, therefore PPD is the sensitizer of prime concern (Jayaganesh et al, 2017).

Contact allergy to p-phenylenediamine (PPD) and other hair materials has become an issue in Europe nowadays. The long-term toxicological risk from semi-permanent hair dyes is low, however, 2-nitro-p-phenylenediamine and 4-nitro-o-phenylenediamine are currently banned in Europe and United States because they have been tested exclusively and proved that both are having the higher potential of carcinogenicity. The sensitization symptoms from oxidation dyes are noticed in discrete dermatitis at the periphery of the scalp and on the edges of the ears and itching scalp, occasionally, eruptions occur on the face, especially around the eyelids. Usually, symptoms appear several hours after the dyeing process, and treatment of this allergic reaction is caused by the oxidation of residual para diamine with peroxide in saline solution and the application of corticoid creams or lotions. Allergic response to temporary hair color rinses is rare, however, a few incidents of allergic reaction to semi-permanent hair dyes have been reported (Jayaganesh et a,2017).

3.2. MECHANISMS/MODE OF ACTION OF COSMETIC ASSOCIATED TOXICITIES.

i. Allergic reactions to cosmetics

Allergic reactions to cosmetics constitute a small but significant portion of the complications associated with the use of cosmetics. Allergic contact dermatitis represents true delayed-type (type IV) hypersensitivity that presents eczematous dermatitis and comprises approximately 10% to 20% of all cases of contact dermatitis. Type IV is a hypersensitivity reaction that is T-cell mediated, wherein circulating or resident sensitized T-cells are activated by the offending allergen to release pro-inflammatory cytokines. Sensitization depends on several factors including product composition, a concentration of potential allergenic components, amount of product applied, site application, skin barrier integrity, and frequency and duration of application. This clinical scenario can range from mild erythema and scale with a minimal itch to vesicular, bullous, indurated plaques that are intensely pruritic. Initial sensitization is required for the subsequent expansion of a reaction when exposure occurs again. Allergic contact urticaria is immediate-type hypersensitivity that represents a true allergic reaction. As the name implies, the reactions occur within minutes to hours and might be limited to the site of exposure on the skin or, in severe cases, reactions can be generalized. Contact urticaria is a rarer reaction to cosmetics and skin care products that may be an immunologic or non-immunologic reaction. It is characterized by the development of a wheal-and-flare response to a topically applied chemical. The spectrum of clinical presentation ranges from itching and burning to generalized urticaria to anaphylaxis. In highly allergic individuals, mucosal exposures, or large exposures, the symptoms of immediate-type hypersensitivity can generalize and include conjunctivitis, cough, bronchoconstriction, hypotension, anaphylaxis, and, occasionally, death (Jonathas et al 2018).

ii. Cancer

Women who used chemical straighteners at least every 5-8 weeks were 30 percent more likely to develop breast cancer. This was a cosmetic practice more commonly used by black women. The study found that 74 percent of black women had used chemical straighteners as opposed to 3 percent of white women. The researchers suggest that this could be because the treatment uses a concoction of chemicals that might include formaldehyde a known carcinogen as an active ingredient (Molly, 2019). Several aromatic amines contained in hair dyes until the 1980s are mutagenic in vitro and carcinogenic in animals and humans. A study identified small amounts of 4-amino-biphenyl, an aromatic amine, which is a recognized human urinary bladder carcinogen, in eight of the 11 hair dyes tested. Darker colors are formed by using higher concentrations of primary intermediates and have been therefore suggested to pose a higher risk of urinary bladder cancer than non-dark-shade hair dyes, although the issue remains open to discussion.

A recent analysis of hair dye use in Los Angeles found a stronger association between hair dye use and bladder cancer risk among subjects with a polymorphism in the detoxifying enzyme N-acetyltransferase 2 (NAT2) that confers a slow acetylation phenotype, compared to those with wild-type or fast acetylator phenotype. At least 1 potentially carcinogenic hair dye ingredient p-phenylenediamine is metabolized by N-acetyltransferase enzymes. Studies consistently find that decreased N-acetyltransferase activity is associated with bladder cancer risk. Future studies that specify the color and type of hair dye, and evaluate factors that influence genetic susceptibility in large study populations will help clarify the potential risk of bladder cancer associated with personal hair dye use (Andrew et al, 2004).

In vitro and animal studies support the carcinogenic potential of certain hair dye constituents. These include 4-methoxy-m-phenylenediamine (4-MMPD, 2,4-diaminoanisole), 4-chloro-m-phenylenediamine, 2,4-toluene diamine, 2-nitro-p-phenylenediamine, and 4-amino-2-nitrophenol. Also, certain azo dyes are metabolized to benzidine, a known human bladder carcinogen. Hair dye components or their derivatives appear in the urine following skin application, indicating that the putative carcinogenic compounds reach the target organ (Andrew et al, 2004). Many hair dyes contain aniline metabolites such as p-aminophenol or m-aminophenol. In cell culture, p-aminophenol induces chromosomal aberrations, complex rearrangement,s, and single-strand DNA breaks, and suppresses the activity of detoxifying enzymes. Hair dyes may contain metallic compounds, in particular lead acetate, cobalt,t, and nickel salts, which are classified as possibly carcinogenic by the International Association for Research on Cancer (IARC). An association between hair dye use and bladder cancer risk is biologically plausible because hair dye components or their derivatives can be found in the urine following application to the skin in human studies, indicating direct exposure of potentially carcinogenic chemicals to the bladder epithelium (Andrew et al, 2004).

iii. Dermatitis

The clinical features of hair dye dermatitis vary from mild contact dermatitis localized to one body site (hand dermatitis) or disseminated generalized dermatitis to severe life-threatening complications such as contact urticaria/angioedema, and rhinitis/bronchospasm/asthma, and renal toxicity. The most common clinical presentations include contact dermatitis localized to sites of contact or photo-exposed skin, periorbital dermatitis, airborne contact dermatitis, hand dermatitis, and rarely erythema multiforme-like lesions. Clinically, characteristic acute (erythematous, edematous, oozy, crusted eczematous plaques), subacute and chronic dermatitis (hyperpigmented, lichenified eczematous lesions) involving multiple sites such as scalp, scalp margins, forehead, eyelids, beard, neck, upper back, and/or hands was observed in all cases(Gupta et al 2015).

PPD provokes cross-allergy, making people allergic to other substances which contain para-substituted amino compounds.

iv. Asthma

Cutaneous reactions, such as dermatitis and urticaria, caused by dyes are widely known. However, only a few reports of bronchial asthma have been reported following the use of dyes.

Volatile antigenic substances are components of hair dyes. These substances probably entered the airways and triggered an asthma attack in our patient. Asthma attacks due to, henna, reactive dye (black B, GR, orange 3R), and carmine have been reported. These causative agents do not only produce local cutaneous reactions, but also cause generalized urticaria, rhinitis, bronchial asthma, and syncope. The mechanism of asthma due to bleach powders containing persulphate salts is unknown. Previous reports have described positive responses to skin tests with persulphate salts, in general at much lower concentrations, in some but not all patients with occupational asthma due to these agents. Specific IgE has not been found in the serum of any patients with respiratory disease due to persulfate salts (Blainley et al 1986).

A rise in serum neutrophil chemotactic activity has been found in various disorders in which allergic mechanisms are an important-for example, allergen-induced asthma, and cold urticaria. While the exact origin of neutrophil chemotactic activity in man remains to be determined, many consider that in vivo neutrophil chemotactic activity is released from mast cells. The significant rise in serum levels of neutrophil chemotactic activity paralleling airflow obstruction suggests that mast cells may play a part in the pathogenesis of the late asthmatic reaction following inhalation of persulphate salts. The mechanism by which mast cell activation may occur in asthma due to persulphates remains unknown. Studies on animal mast cell preparations have shown that persulphate salts can release histamine directly (Blainley et al 1986).

v. Hormone Imbalance

Parabens mimic your estrogen and are readily stored in your body fat. Parabens easily penetrate your skin and are suspected to interfere with your hormone function. Parabens interfere with the estrogen-activating enzyme 17β-hydroxysteroid dehydrogenase (17β-HSD) 1 and the estrogen-inactivating 17β-HSD2, parabens possess excellent chemical stability and are biodegradable. Chemically, parabens are alkyl esters of p-hydroxybenzoic acid of which propyl- and methylparaben are the most frequently used parabens in cosmetic products. Parabens are very rapidly metabolized to p-hydroxybenzoic acid by esterases in the liver and the skin, followed by excretion via the urine. Parabens are mainly excreted as glycine, sulfate, and glucuronide conjugates. The topical application of paraben-containing products more likely contributes to the systemic paraben concentration than their oral intake due to the rapid intestinal and hepatic metabolism (Roger et al., 2017).

In 2004, Darbre et al. reported the detection of unconjugated parabens in breast cancer tissue, triggering further investigations into estrogenic activities of parabens. Estrogens are primary female sex hormones playing a central role in a variety of physiological actions in females and males. In females, estrogens primarily regulate the sexual development of the reproductive tissues and the development of secondary sexual characteristics at puberty. Estrogens trigger target gene expression mainly by acting through estrogen receptors α and β (ERα, ERβ). The 17β-hydroxysteroid dehydrogenase types 1 and 2 (17β-HSD1 and 17β-HSD2) regulate the local balance between potent and weakly active estrogens. While 17β-HSD1 converts the weakly active estrone (E1) into the most potent estrogen estradiol (E2), 17β-HSD2 catalyzes the opposite reaction and decreases the local concentrations of active estrogens. Thus, compounds inhibiting 17β-HSD2 result in increased local active estrogen concentrations and can increase the transcription of estrogenic target genes, thereby causing estrogenic effects. Conversely, compounds inhibiting 17β-HSD1 possess anti-estrogenic properties by reducing local active estrogen concentrations. A high 17β-HSD2 to 17β-HSD1 ratio in ERα-positive breast cancer patients has been shown to positively correlate with the survival of ERα-positive patients. This finding illustrates the importance of proper 17β-HSD2 function (Roger et al., 2017).

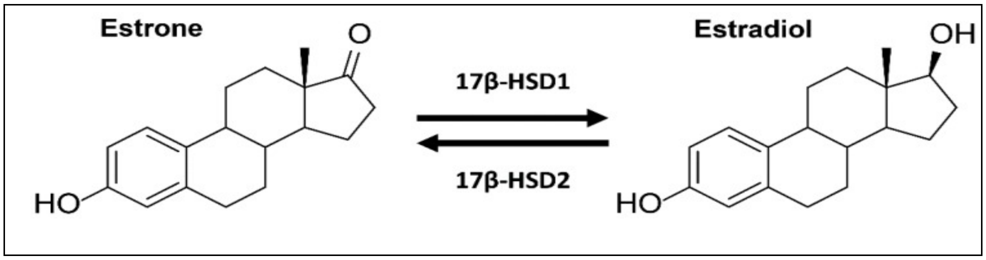

Figure 10: Interconversion of potent (estradiol) and weakly active estrogens (estrone) by 17β-hydroxysteroid dehydrogenase (17β-HSD) enzymes (Roger et al., 2017).

Parabens, as well as methyl vanillate, ethyl vanillate, ethyl gallate, and butyl gallate inhibited 17β-HSD2 at a concentration of 20 µM. The common paraben metabolite p-hydroxybenzoic acid was inactive.Small parabens such as the main metabolite p-hydroxybenzoic acid, methyl-, and ethylparaben did not inhibit 17β-HSD1. In contrast larger parabens size-dependently inhibited 17β-HSD1 activity; vanillate, ethyl vanillate, ethyl gallate and butyl gallate did not inhibit 17β-HSD1 (Roger et al., 2017).

vi. Weakening of hair cuticle

The intended desirable effects of cosmetics on hair are very wide and variable. Some desirable actions of hair cosmetics are not achievable without inducing some kind of damage to the hair fiber itself, e.g, in permanent or oxidative hair dyeing a degree of damage to the hair cuticle is necessary to introduce the dyes that are targeting the hair cortex. The same is true for bleaching and perming. When the hair cuticle is weakened it cannot be fully restored (Fig. 15), but some cosmetic agents may decrease the abnormal fragility and the rough feel of damaged hair. No better results can be achieved than by cutting away the damaged fibers and letting new hair growth proceed without new harsh procedures (Fig. 16) (Barel et al., 2001).

Hair cosmetics and shampoos in particular are formulated to be nontoxic, nonirritant, and non-damaging to the hair, skin, and eyes. These formulae should not of course, include substances that are systemically toxic following their percutaneous absorption. The integrity of the cuticle is degraded by perming, bleaching, and permanent dyeing, which lead to raising and softening of the cuticle thereby making it vulnerable to mechanical abrasion,e.g., during combing.Scalp hair may be under excessive physical traction determined by fashion, e.g.,tight rollers and tight hairstyles. This can result in temporary hair loss, and if continued over a long period will result in permanent hair loss (thinning). Some examples of this condition have been described by medical literature as chignon alopecia and frontoliminal alopecia (Barel et al, 2001).
The hair shaft can be damaged by previous permanent waving or bleaching and thus made more permeable to certain dyes, leading to some unexpected effects, e.g., greencolor from azo dyes, green hair from copper metallic salts, and red hair from chino form. The so-called Bird′s Nest hair is a physical phenomenon of felting. This occurs when frictional forces are applied to physically damaged hair especially after the use of a cationic shampoo. A large tangled mass of qhair is produced and defies all attempts to unravel it, and the mass has to be cut off. The process can be reproduced experimentally with normal hair. There is no evidence that subjects affected have especially susceptible hair (Barel et al., 2001).

Figure 12: Trichoptilosis or split ends. These

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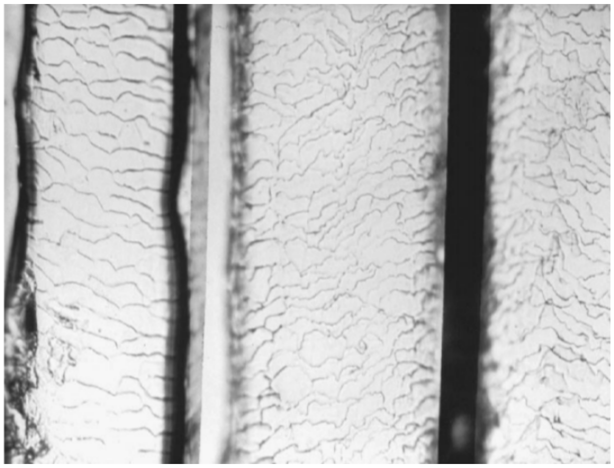
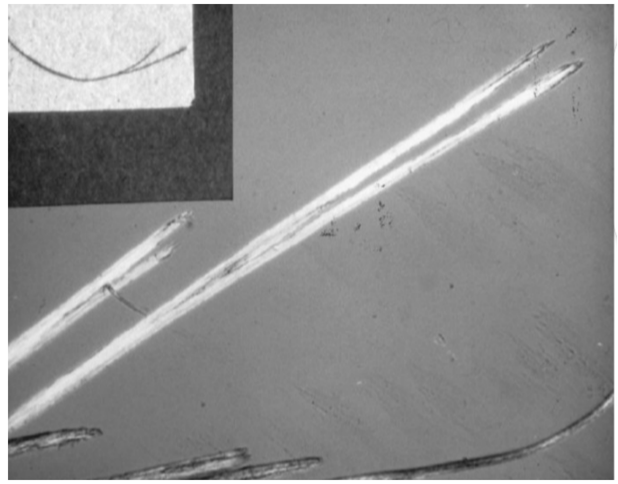


Figure 11: The condition of the cuticle on three hair segments taken at the merger of the scalp(left), 1cm away from it(middle), and 3cm away (right). Damage of the cuticular scale edges clearly occurs within 3-4 months of exposure to the environment.(Barel et al, 2001).



damaged hair tips frequently occur on long hairs, lack of cuticle which normally envelopes the hair fibre, exposes the cortex a much weaker part of the hair shaft (Barel et al, 2001).

4. THERAPIES FOR COSMETIC ASSOCIATED TOXICITIES.

4.1. In acute severe cases of PPD hair dye dermatitis

•Wash the hair and scalp thoroughly with a mild soap or soapless shampoo to remove the excess dye

•Apply a 2% hydrogen peroxide solution or compresses of potassium permanganate in a 1:5000 dilution to completely oxidise the PPD

•To soothe, soften the crust, and alleviate the tight feeling of the scalp, apply a wet dressing of cold olive oil and lime.

•Further treatment with a topical application of an emulsion of water and water-miscible corticosteroid cream, or oral corticosteroids may be indicated. Management of PPD dermatitis on other parts of the body may be treated as acute dermatitis; this may include treatment with topical corticosteroids and emollients

4.2. Suggestions in the development of non-toxic cosmetics

Biological compounds, besides medical, pharmaceuticals and food industries, have mottled application in cosmetic industries. Many biological molecules, directly or indirectly, have found key role in the production of various compounds, like esters, aroma compounds and active agents, far and wide used in cosmetic industries. The major advantage of using microbial ingredients is its biocompatibility; additionally, they do have other benefits like simplified process, improved and consistent quality of product and environmental footprint. Of several, microbes, bacteria secrets copious biologically active compounds with significant commercial values; to mention few Oligosaccharides, Exopolysaccharides (EPS), Biosurfactants, Enzymes, Peptides, Vitamins etc. These compounds, replacing chemical compounds, found their application in various cosmetic products used either for beautification or for improving health of the target (Prabhuddha et al., 2019).

i. Oligosaccharides

Cyclodextrins, are a group of compounds made up of cyclic oligosaccharides with α-(1,4) linked glucopyranose moiety bound together in a ring and have noteworthy contribution in cosmetic formulations. Cyclodextrin, majorly, is used to reduce the volatility of esters in perfumes and room freshener gels. Cyclodextrin powders, of smaller size, are used as odor control in talcum, diapers, menstrual discs, pads, napkins, etc. The commercial production of cyclodextrin is more popular by enzymatic transformation rather than chemical synthesis. Therefore, the production of cyclodextrinase enzyme has been extensively carried out by using bacteria strains. Bacillus subtilis Strain 313, Brevibacterium sp. Strain 9605, Brevibacillus brevis Strain CD 162, Microbacterium terrae KNR 9 are some of the prominent strains used for the production of cyclodextrin. Cyclodextrin glucanotransferase (EC 2.4.1.19) obtained from alkalophilic Bacillus agaradhaerensis is a widely sought enzyme in the potential cosmetic preparations (Prabhuddha et al., 2019).

ii. Exopolysaccharides

The distinctive biocompatibility and non-toxic nature of microbial exopolysaccharides (EPS) has helped considerably to exploit its use in cosmetic industry. Moreover, hydrophilic EPS have high water retention ability which helps to maintain a hydrated environment in skin formulations. One of the very well know EPS produced from glucose polymer is dextran. Dextran is obtained from Leuconostocaceae family of microbes such as Leuconostoc mesenteriodes and Streptococcus mutans. In cosmetics dextran is used as skin smoothing and brightening agent, as it promotes the firmness of skin, promotes radiance, and reduce the appearance of wrinkles. Dextrans also has anti-inflammatory property as it improves the blood flow, augmented nitric oxide (NO) synthesis in the human epidermal keratinocytes cells (Prabhuddha et al., 2019).

iii. Proteins, Enzymes and Peptides

In addition to biosurfactants, proteins and peptides also have contributed significantly in the cosmetic industry. Proteins and peptides, since ancient time, are used for improving the quality of the skin, hair or nails. Extensive research has been carried out in the same horizon and identified numerous applications of proteins in the cosmetic industry.Superoxide dismutase (SOD) and Peroxidase (catalase, glutathione peroxidases, lactoperoxidases) works synergistically as exfoliate. These enzymes serve as scavengers of free radicals and prevent the skin, from the ultra violet light, when applied on the skin surface. Similar enzyme Lactate dehydrogenase (LDH) capable of catalyzing the reduction of NADH and pyruvate leading to NAD+ and lactate as the end product. The above reaction, on the exposure of UV, gets diminished; but, in presence of LDH the subunits remain intact in the cells and allow cell to carry out normal functioning (Prabhuddha et al., 2019).

The commonly used ingredient Sericin protein in hair conditioning and skin formulations, is generally produced by Bombix mori (Silk worm), and can also alternatively obtained from microalgae Chlorella vulgaris and Arthrospira platensis. 7-phloroeckol are validated to promote stimulation of hair growth in dermal papilla cells (DPCs) and outer root sheath cells (ORS). Algal oil rich in omega-3 is known for its ability to reduce dry and brittle hair, scratchy and itchy scalp, decrease dandruff, and hair fall. Microalgae derived Docosahexaenoic Acid (DHA) and Eicosapentaenoic acid (EPA), regularly used in hair oils, hair serum, hair gels and spray, provide deep nourishment to the hair follicles and scalp to make the hair strong and healthier (Prabhuddha et al., 2019).

There are many alternatives to toxic chemicals used in the production of cosmetic which are very effective and safe, some non-toxic alternative to toxic chemicals used in cosmetic preparation are listed below;

Parabens alternatives are; Vitamin E, rosemary extract, fermented radish root, grapefruit seed extract, sodium benzoate, and antioxidant oils such as almond, avocado, and hemp seed oil.

Petroleum and mineral oil alternatives are; Natural moisturizers such as vegetable glycerin, coconut oil, sunflower oil, olive oil, raw honey, and shea butter.

Aloe vera (contains proteolytic enzymes good for healing scalp problems and stimulating hair growth)

Avocado (dermatological benefits for scalp, with vitamins A, D, and E; effectively lubricates hair strand, preventing breakage)

Shea butter (a hydrating emollient; protects the hair strand)

Castor oil (antifungal; cleans the scalp, clearing follicles and promoting hair growth)

Coconut oil (a hydrating emollient that seals moisture around the hair follicle)

Extra virgin olive oil (a hydrating emollient and moisturizer, effective at softening hair)

Grape seed (lightweight conditioner and moisturizer; mildly astringent, thus effective at fighting dandruff; easily absorbs into hair and scalp and is packed with healthy fatty acids)

Honey (humectant and antifungal)

Jojoba (hair strengthener, rich in vitamins C, E, and B; dermatological benefits for repairing scalp dryness and inflammation)

5. CONCLUSION

The study has shown that there are diverse toxicological implication of using cosmetics on human health, one of the most prevailing toxic chemicals found in most cosmetic products is PPD(P-Phenyladiamine) and BHA(Butylated Hydroxyanisole).

The cosmetic products may present health risks and recurrent adverse effects are attributed to the toxic substances commonly found in their formulations. Although the various structures for the regulation and quality control of cosmetics around the world are quite complex and comprehensive, they should be more rigorous in the inclusion of new substances with toxic potential in the formulation of cosmetics to avoid damages to human health.

To encourage improvements in the manufacture, marketing and use of cosmetic products by the population, it is necessary to apply a unified cosmetovigilance around the world. This public health strategy are a genuine means of obtaining information on the safety of cosmetic products and their ingredients, preventing the risks associated with using cosmetics become a serious public health problem.

6. RECOMMENDATIONS

The following are recommended:

1. Detailed research should be carried out on the effects of these toxic chemicals used in production of most cosmetics on biochemical parameters.
2. Extensive public sensitization should be carried out to enlighten cosmetics users on the toxicity content of chemicals used in production of cosmetics.
3. Appropriate means for treatment of cosmetic induce toxicity should be put in place.
4. The National Centre for Biotechnology Information (NCBI), National Library of Medicine (NLM), National Institute of Health (NIH) and the World Health Organization (WHO) should conduct series of comprehensive surveys on cosmetics.
5. The Standard Organization of Nigeria (SON), National agency for food and drug administration control (NAFDAC) should regulate the production of cosmetics and organize quality checks on cosmetics products.

7. APPENDIX

ACGIH - American Conference of Governmental Industrial Hygienists.

BHA - Butylated Hydroxyanisole.

BHT - Butylated Hydroxytoluene.

CDC - Center for Disease Control.

DEA - Diethanolamine.

DHA - Docosahexaenoic Acid.

DPC - Dermal Papilla Cells.

EPA - Eicosapentaenoic Acid.

EPS - Exopolysaccharides.

IARC - International Agency for Research on Cancer.

LDH - Lactate dehydrogenase.

NAFDAC - National Agency for Food and Drug Administration Control.

NTP - National Toxicology Program.

ORS - Outer Root Sheath Cells.

PMS - Post Market Surveillance.

PPD - P-Phenylenediamine.

PPD - Persistent Pigment Darkening.

SOD - Superoxide Dismutase.

TEA - Triethanolamine.

TWA - Time Weight Average.

UV - Ultra Violent Ray.

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